REMARKS/ARGUMENTS

Claims 1-12 remain pending.

The suggestions provided in the Action at page 3 have been partly adopted and therefore the rejection under 112, 2nd paragraph is no longer applicable. Further support is find on page 9, lines 27-28.

No new matter is added.

The rejection of Claims 1 and 3 to 10 under 35 U.S.C. 102(b) citing Okarma (US 6,143,508) is not applicable to the claims because (A) Okarma does not actually teach that stem cells are to be treated in the manner outlined in the rejection; and (B) Okarma does not describe mechanical AND enzymatic dissolution as set forth in the claims.

Okarma describes methods, compositions and devices for the separation of certain cell populations from a mixture of cells, The methods described by Okarma are based on the capture of the cells of interest, through ligand/receptor interactions, followed by the releasing of the captured cells (see, e.g., col. 2, lines 15-29).

The method of Claim 1 for preparing stem cells, includes four steps; (i) cell extraction; (ii) mechanical dissociation; (iii) enzymatic dissociation; and (iv) maintaining of the cells obtained in a specific medium.

The rejection largely picks and chooses separate parts of the Okarma reference that really have nothing to do with each other but for being in the same specification. The only stem cells mentioned by Okarma are obtained from bone marrow or peripheral blood (col. 8, lines 46-47, cited by the Examiner). Such cells obtained either from bone marrow or peripheral blood are in suspension, and certainly not "held together by a membranous or other connecting material." Hence, neither Okarma provides nor would one apply such stem cells a dispersion treatment as recited in col. 4, lines 25-30 (cited in the rejection).

Okarma describes the possibility of dispersing the cells either mechanically OR enzymatically (see col. 4, lines 25-30) but does not describe mechanical AND enzymatic dissociation. . Since claims 2-4, 7 and 10 depend on claim 1, they are also not anticipated by Okarma. The notation in the Action for the inclusion of claims 5, 6, and 8 in the rejection should no longer be applicable in light of the clarifying amendments submitted here.

Withdrawal of the rejection is requested.

The rejection of Claims 1, 3-4 and 6-9 under 35 U.S.C. 102(b) citing Mignone et al. (W0200l/3 6482) is not applicable to the claims because Migonne does not describe maintaining cells in a specific culture medium for preserving diversity and plasticity of the stem cells.

Mignone et al. describe non-human transgenic mammals expressing a marker/reporter protein under the control of a particular regulatory sequence. In example 8, they describe neuronal transplant experiments which have been performed by inserting, into the brain of a rat, transgenic cells obtained from a mouse transgenic embryo.

In this Example 8, Mignone et al. enzymatically digests the cells (trypsin), triterated with a pipette and then washed/pelleted in DMEM/F12 to remove the trypsin. The cells are maintained (kept on ice) in HBSS (short for Hank's Buffered Saline Solution)--see page 30, lines 1-9- before injecting them into the rat brain. HBSS is a salt solution, which has the following composition: 0.137 M NaCl; 5.4 mM KCl; 0.25 mM Na_2HPO_4, 0.44 mM KH_2PO_4, 1.3 mM $CaCl_2$, 1.0 mM $MgS0_4$ 4.2 mM $NaHCO_3$.

HBSS is not a culture medium and certainly not a "specific culture medium for preserving diversity and plasticity of stem cells" as set forth in the claims. Maintaining the cells in HBSS more than a few minutes would result in cell death. As appears page 30, lines 6-7 of Mignone et al., the cells were kept in HBSS only during the time necessary to have the

recipient rat ready for cellular transfer. It appears from page 30, lines 7-26, that this preparation was very simple and rapid, and hence that cells have been kept in HBSS during only a very short while (no more than a few minutes).

Withdrawal of the rejection is requested.

The rejection of Claims 1 and 3-9 under 35 U.S.C. 102(b) citing DiMario et at. (Experimental Cell Research, 1995) is not applicable to the claims because DiMario do not describe maintaining cells in a specific culture medium for preserving diversity and plasticity of the stem cells because, in fact, DiMario describes that in their experiments the cells obtained were not so preserved.

DiMario et al. transplanted myoblasts having undergone different treatments into limb buds of chick embryos, to determine the conditions that affect the ability of transplanted cells to populate newly developing limb musculature (see Abstract). DiMario describe that myoblasts which have been freshly isolated and transplanted without any culture step formed more fibres than the same myoblast type which had been maintained in cell culture (sentence bridging the two columns of page 436). In the discussion, DiMario state that this was due to the fact that "over time, a portion of the myoblasts maintained in vitro irreversibly differentiate before injection". (page 441, lines 25-26)

Thus, DiMario et al. do not describe any step corresponding to step (iv) of the method according to claim 1 (i.e., maintaining of the cells obtained in a specific culture medium for preserving diversity and plasticity). To the contrary, DiMario teach that cells cannot be maintained in a cell culture medium without losing their plasticity and diversity. (page 441, lines 25-26).

The notation in the Action for the inclusion of claims 6 and 8 in the rejection should no longer be applicable in light of the clarifying amendments submitted here.

Withdrawal of the rejection is requested.

The rejection of Claims 1 and 3-9 under 35 U.S.C. 102(b) citing Pouzet et al. (Circulation, 2000) because Pouzet do not describe maintaining cells in a specific culture medium for preserving diversity and plasticity of the stem cells because, in fact, Pouzet describes that in their experiments the cells obtained were not so preserved.

Pouzet et al. disclose results of a study designed to determine whether culture of myoblasts could be bypassed when performing autologous skeletal myoblast transplantation in infracted myocardium. Pouzet compared the functional results obtained with myoblasts which have been expanded in culture in F 12 medium with 20% PBS ("Myoblasts" group) to those obtained with myoblasts which have only been obtained by muscle mincing and kept in P12 medium ("Mincing" group) (see Abstract, pp. III-211 "Experimental Groups" 2nd col). Further, in the "Mincing" group, the myoblasts were kept in F12 medium without PBS (see page II-211, 2nd col," Muscle Mincing Methodology").

Pouzet et al. results show that the "Mincing" group failed to provide functionally effectiveness (see figure 3). Further, Pouzet state quite clearly that cell expansion is required (see page III-213, second col. 1st para of the Discussion) and that mincing did not work (see page III-214, 2nd col. last two paragraphs: " . . .a theoretically attractive approach of mincing ... thought to increase the likelihood of graft survival . . these expectations were not met by the results. . . "

Therefore, Pouzet makes it clear that the P12 medium used to maintain the myoblasts is not a "specific culture medium for preserving diversity and plasticity"

The notation in the Action for the inclusion of claims 6 and 8-9 in the rejection should no longer be applicable in light of the clarifying amendments submitted here.

Withdrawal of the rejection is requested.

The rejection of Claims 1 to 12 under 35 U.S.C. 103(a) citing Pouzet et al. and DiMario et al cannot be applicable as well because as already explained for each of these references above, neither describes maintaining cells in a specific culture medium for preserving diversity and plasticity of the stem cells because, in fact, both Pouzet and DiMario describe that in their experiments the cells obtained were not so preserved..

Further, Pouzet et al. teach away from maintaining cells as in the claims because Pouzet makes it clear that *in vitro* cell expansion is mandatory for skeletal myoblast transplantation to be effective.

Claims 5, 6, 8 and 9 pertain to products comprising at least stem cells obtained by the method according to claim 1, said cells being in a specific medium devoid of animal serum, wherein said medium comprises at least a) a nutritive medium; b) a protective factor; c) hormones; and d) differentiation inhibiting factors. The Examiner has considered that both DiMario and Pouzet teach 3 of the four recited components, and that it would have been obvious for the person of ordinary skill in the art at the time the invention was made, to modify the media described in these documents to obtain stem cells in a medium as defined in claim 2. The Examiner has considered that the components of the specific culture medium of claim 2 were commonly known and used within the art of tissue culture for maintaining viability of cells.

The amendments made to claims 5, 6 and 8, especially the specification that the medium is devoid of animal serum, should obviate this rejection, since nothing in Pouzet et al. nor in DiMario et al. suggests to reconstitute a culture medium for preserving the diversity and plasticity of stem cells by combining the recited components. While some of the components were commonly known and used in the art of tissue culture, the combination of these components, such as in the claims, was not suggested in the prior art, and was not

obvious for the skilled artisan at the time the invention was made, especially for maintaining stem cells.

Withdrawal of the rejection is requested.

A Notice of Allowance is also requested.

Respectfully submitted,

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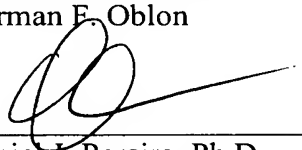

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